

In the Claims

This listing of claims will replace all prior versions and listings of claims in the application.

Please amend claims 13 and 21 and add new claims 121 and 122, as indicated below:

1. (canceled)
2. (withdrawn) The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid molecule codes for SEQ ID NO:3.
3. (withdrawn) The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid molecule comprises the nucleotide sequence set forth as SEQ ID NO:1.
4. (withdrawn) The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid molecule comprises a nucleotide sequence set forth as SEQ ID NO:2.
5. (withdrawn) An isolated TLR9 polypeptide or fragment thereof comprising at least one amino acid of murine TLR9 selected from the group consisting of amino acids 2, 3, 4, 6, 7, 18, 19, 22, 38, 44, 55, 58, 61, 62, 63, 65, 67, 71, 80, 84, 87, 88, 91, 101, 106, 109, 117, 122, 123, 134, 136, 140, 143, 146, 147, 157, 160, 161, 167, 168, 171, 185, 186, 188, 189, 191, 199, 213, 217, 220, 227, 231, 236, 245, 266, 269, 270, 271, 272, 273, 274, 278, 281, 285, 297, 298, 301, 305, 308, 311, 322, 323, 325, 326, 328, 332, 335, 346, 348, 353, 355, 358, 361, 362, 365, 367, 370, 372, 380, 381, 382, 386, 389, 392, 394, 397, 409, 412, 413, 415, 416, 419, 430, 432, 434, 435, 438, 439, 443, 444, 446, 447, 448, 450, 451, 452, 454, 455, 459, 460, 463, 465, 466, 468, 469, 470, 472, 473, 474, 475, 478, 488, 489, 494, 495, 498, 503, 508, 510, 523, 531, 539, 540, 543, 547, 549, 561, 563, 565, 576, 577, 579, 580, 587, 590, 591, 594, 595, 597, 599, 601, 603, 610, 611, 613, 616, 619, 632, 633, 640, 643, 645, 648, 650, 657, 658, 660, 667, 670, 672, 675, 679, 689, 697, 700, 703, 705, 706, 711, 715, 716, 718, 720, 723, 724, 726, 729, 731, 735, 737, 743, 749, 750, 751, 752, 754, 755, 759, 760, 772, 774, 780, 781, 786, 787, 788, 800, 814, 821, 829, 831,

832, 835, 844, 857, 858, 859, 862, 864, 865, 866, 879, 893, 894, 898, 902, 910, 917, and 927 of SEQ ID NO:3, wherein the TLR9 polypeptide or fragment thereof has an amino acid sequence which is identical to a human TLR9 polypeptide or fragment thereof except for the at least one amino acid of murine TLR9.

6. (withdrawn) The isolated TLR9 polypeptide or fragment thereof of claim 5, further comprising at least one amino acid of murine TLR9 selected from the group consisting of amino acids 949, 972, 975, 976, 994, 997, 1000, 1003, 1004, 1010, 1011, 1018, 1023, and 1027 of SEQ ID NO:3.

7. (withdrawn) The isolated TLR9 polypeptide or fragment thereof of claim 5, wherein the human TLR9 has an amino acid sequence set forth as SEQ ID NO:6.

8. (withdrawn) The isolated TLR9 polypeptide or fragment thereof of claim 5, wherein the isolated TLR9 polypeptide or fragment thereof has an amino acid sequence selected from the group consisting of SEQ ID NO:3 and fragments of SEQ ID NO:3.

9. (withdrawn) The isolated TLR9 polypeptide or fragment thereof of claim 5, wherein the isolated TLR9 polypeptide or fragment thereof is an extracytoplasmic domain of TLR9.

10. (withdrawn) The isolated TLR9 polypeptide or fragment thereof of claim 5, wherein the isolated TLR9 polypeptide or fragment thereof comprises an MBD motif as set forth as SEQ ID NO:126 or SEQ ID NO:127.

11. (withdrawn) The isolated TLR9 polypeptide or fragment thereof of claim 5, wherein the isolated TLR9 polypeptide or fragment thereof selectively binds to an immunostimulatory nucleic acid (ISNA).

12. (withdrawn) The isolated TLR9 polypeptide or fragment thereof of claim 5, wherein the isolated TLR9 polypeptide or fragment thereof selectively binds to a CpG nucleic acid.

13. (currently amended) An isolated nucleic acid molecule which encodes a Toll-like receptor 9 (TLR9) polypeptide hTLR9-CXXCm, said polypeptide comprising an amino acid sequence of SEQ ID NO:6 except for substitution of amino acids 269-274 (PRHFPQ) of SEQ ID NO:6 with amino acids 269-274 (GQKSLH) of SEQ ID NO:3.

14. (canceled)

15. (canceled)

16. (withdrawn) The host cell of claim 15, further comprising at least one expression vector selected from the group consisting of:

- (a) an expression vector comprising a nucleic acid molecule which encodes an isolated TLR7 polypeptide operably linked to a promoter, and
- (b) an expression vector comprising a nucleic acid molecule which encodes an isolated TLR8 polypeptide operably linked to a promoter.

17. (canceled)

18. (original) An expression vector comprising the isolated nucleic acid molecule of claim 13 operably linked to a promoter.

19. (original) A host cell comprising the expression vector of claim 18.

20. (withdrawn) The host cell of claim 19, further comprising at least one expression vector selected from the group consisting of:

- (a) an expression vector comprising a nucleic acid molecule which encodes an isolated TLR7 polypeptide operably linked to a promoter, and
- (b) an expression vector comprising a nucleic acid molecule which encodes an isolated TLR8 polypeptide operably linked to a promoter.

21. (currently amended) The host cell of claim 19, further comprising a reporter gene construct ~~to detect Toll-like receptor (TLR)-related signaling comprising a reporter gene operatively linked to a promoter sensitive to NF-κB.~~

22. (withdrawn) An isolated nucleic acid molecule selected from the group consisting of

- (a) nucleic acid molecules which hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence set forth as SEQ ID NO:173, and which code for a murine TLR7 having an amino acid sequence set forth as SEQ ID NO:175,
- (b) nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to degeneracy of the genetic code, and
- (c) complements of (a) or (b).

Claims 23-25 (canceled)

26. (withdrawn) An isolated TLR7 polypeptide or fragment thereof comprising at least one amino acid of murine TLR7 selected from the group consisting of amino acids 4, 8, 15, 16, 18, 21, 23, 24, 25, 27, 37, 39, 40, 41, 42, 44, 45, 61, 79, 83, 86, 89, 92, 96, 103, 109, 111, 113, 119, 121, 127, 128, 131, 145, 148, 151, 164, 172, 176, 190, 202, 203, 204, 205, 222, 225, 226, 228, 236, 238, 243, 250, 253, 266, 268, 271, 274, 282, 283, 287, 288, 308, 313, 314, 315, 325, 328, 331, 332, 341, 343, 344, 347, 351, 357, 360, 361, 362, 363, 364, 365, 366, 370, 371, 377, 378, 387, 388, 389, 392, 397, 398, 413, 415, 416, 419, 421, 422, 425, 437, 438, 440, 446, 449, 453, 454, 455, 456, 462, 470, 482, 486, 487, 488, 490, 491, 493, 494, 503, 505, 509, 511, 529, 531, 539, 540, 543, 559, 567, 568, 574, 583, 595, 597, 598, 600, 611, 613, 620, 624, 638, 645, 646, 651, 652, 655, 660, 664, 665, 668, 669, 672, 692, 694, 695, 698, 701, 704, 714, 720, 724, 727, 728, 733, 738, 745, 748, 755, 762, 777, 780, 789, 803, 846, 850, 851, 860, 864, 868, 873, 875, 884, 886, 888, 889, 890, 902, 903, 911, 960, 967, 970, 980, 996, 1010, 1018, 1035, and 1045 of SEQ ID NO:175, wherein the TLR7 polypeptide or fragment thereof has an amino acid sequence which is identical to a human TLR7 polypeptide or fragment thereof except for the at least one amino acid of murine TLR7.

Claims 27-39 (canceled)

40. (withdrawn) An isolated nucleic acid molecule selected from the group consisting of
- (a) nucleic acid molecules which hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence set forth as SEQ ID NO:190, and which code for a murine TLR8 having an amino acid sequence set forth as SEQ ID NO:192,
 - (b) nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to degeneracy of the genetic code, and
 - (c) complements of (a) or (b).

Claims 41-43 (canceled)

44. (withdrawn) An isolated TLR8 polypeptide or fragment thereof comprising at least one amino acid of murine TLR8 selected from the group consisting of amino acids 5, 6, 9, 10, 14, 15, 18, 21, 22, 23, 24, 25, 26, 27, 28, 30, 39, 40, 41, 43, 44, 50, 51, 53, 55, 61, 67, 68, 74, 80, 85, 93, 98, 99, 100, 104, 105, 106, 107, 110, 114, 117, 119, 121, 124, 125, 134, 135, 138, 145, 155, 156, 157, 160, 161, 162, 163, 164, 166, 169, 170, 174, 180, 182, 183, 186, 187, 191, 193, 194, 196, 197, 199, 200, 207, 209, 210, 227, 228, 230, 231, 233, 234, 241, 256, 263, 266, 267, 268, 269, 272, 274, 275, 276, 280, 285, 296, 298, 299, 300, 303, 305, 306, 307, 310, 312, 320, 330, 333, 335, 343, 344, 345, 346, 347, 349, 351, 356, 362, 365, 366, 375, 378, 379, 380, 381, 383, 384, 386, 387, 392, 402, 403, 408, 414, 416, 417, 422, 426, 427, 428, 429, 430, 431, 433, 437, 438, 439, 440, 441, 444, 445, 449, 456, 461, 463, 471, 483, 486, 489, 490, 494, 495, 496, 505, 507, 509, 512, 513, 519, 520, 523, 537, 538, 539, 541, 542, 543, 545, 554, 556, 560, 567, 569, 574, 575, 578, 586, 592, 593, 594, 595, 597, 599, 602, 613, 617, 618, 620, 621, 623, 628, 630, 633, 639, 641, 643, 644, 648, 655, 658, 661, 663, 664, 666, 668, 677, 680, 682, 687, 688, 690, 692, 695, 696, 697, 700, 702, 703, 706, 714, 715, 726, 727, 728, 730, 736, 738, 739, 741, 746, 748, 751, 752, 754, 757, 764, 766, 772, 776, 778, 781, 784, 785, 788, 791, 795, 796, 801, 802, 806, 809, 817, 820, 821, 825, 828, 829, 831, 839, 852, 853, 855, 858, 863, 864, 900, 903, 911, 918, 934, 977, 997, 1003, 1008, 1010, 1022, 1023, 1024, 1026, and 1030 of SEQ ID NO:192, wherein the TLR8 polypeptide or fragment thereof has an amino acid sequence which is identical to a human TLR8 polypeptide or fragment thereof except for the at least one amino acid of murine TLR8.

Claims 45-61 (canceled)

62. (withdrawn) A method for identifying nucleic acid molecules which interact with a TLR polypeptide or a fragment thereof, comprising:

contacting a TLR polypeptide selected from the group consisting of TLR7, TLR8, TLR9, and nucleic acid-binding fragments thereof with a test nucleic acid molecule; and

measuring an interaction of the test nucleic acid molecule with the TLR polypeptide or fragment thereof.

Claims 63-79 (canceled)

80. (withdrawn) A screening method for identifying an ISNA, comprising:

contacting a functional TLR selected from the group consisting of TLR7, TLR8, and TLR9 with a test nucleic acid molecule;

detecting presence or absence of a response mediated by a TLR signal transduction pathway in the presence of the test nucleic acid molecule arising as a result of an interaction between the functional TLR and the test nucleic acid molecule; and

determining the test nucleic acid molecule is an ISNA when the presence of a response mediated by the TLR signal transduction pathway is detected.

Claims 81-97 (canceled)

98. (withdrawn) A screening method for comparing TLR signaling activity of a test compound with an ISNA, comprising:

contacting a functional TLR selected from the group consisting of TLR7, TLR8, and TLR9 with a reference ISNA and detecting a reference response mediated by a TLR signal transduction pathway;

contacting a functional TLR selected from the group consisting of TLR7, TLR8, and TLR9 with a test compound and detecting a test response mediated by a TLR signal transduction pathway; and

comparing the test response with the reference response to compare the TLR signaling activity of the test compound with the ISNA.

Claims 99-113 (canceled)

114. (withdrawn) A screening method for identifying species specificity of an ISNA, comprising:

- contacting a functional TLR selected from the group consisting of TLR7, TLR8, and TLR9 of a first species with a test ISNA;
- contacting a functional TLR selected from the group consisting of TLR7, TLR8, and TLR9 of a second species with the test ISNA;
- measuring a response mediated by a TLR signal transduction pathway associated with the contacting the functional TLR of the first species with the test ISNA;
- measuring a response mediated by the TLR signal transduction pathway associated with the contacting the functional TLR of the second species with the test ISNA; and
- comparing (a) the response mediated by a TLR signal transduction pathway associated with the contacting the functional TLR of the first species with the test ISNA with (b) the response mediated by the TLR signal transduction pathway associated with the contacting the functional TLR of the second species with the test ISNA.

Claims 115-119 (canceled)

120. (withdrawn) A method for identifying lead compounds for a pharmacological agent useful in treatment of disease associated with TLR9 signaling activity, comprising

- providing a cell comprising a TLR9 as provided in claim 5;
- contacting the cell with a candidate pharmacological agent under conditions which, in the absence of the candidate pharmacological agent, cause a first amount of TLR9 signaling activity; and
- determining a second amount of TLR9 signaling activity as a measure of the effect of the pharmacological agent on the TLR9 signaling activity, wherein a second amount of TLR9 signaling activity which is less than the first amount indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which reduces TLR9 signaling activity

and wherein a second amount of TLR9 signaling activity which is greater than the first amount indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which increases TLR9 signaling activity.

121. (new) The host cell of claim 19, wherein the host cell is a 293 fibroblast cell.

122. (new) The host cell of claim 21, wherein the host cell is a 293 fibroblast cell.